

T3-00003

Application Number: T3-00003

Scientific Score: 60 or below

Specific names of individuals and institutions are blacked out to preserve applicant confidentiality where possible.

Title: Role of microenvironment in regulation of stem cell fate and development of disease

Proposal Abstract as Submitted by Applicant

We propose a specialized Type III training program to provide 3 years of training for 4 post doctoral fellows. Stem cell fate is regulated by multiple signals provided by the local microenvironmental niche. Knowledge of the structure and function of the regulatory niche is crucial for understanding stem cell biology under physiological and pathological conditions. Our emphasis on the role of the niche in the regulation of stem cells is distinct and complementary to programs from other institutes. Courses will provide cutting edge information in the field of the stem cell regulatory niche. Year 1: Cellular and molecular biology of different lineage- and organ- specific niches. Year 2: The role of microenvironment in the development of inflammatory diseases, obesity and cancer. Year 3: Therapeutic approaches targeting stem cell niches including cell transplantation, niche reconstruction methodologies and gene transfer approaches. Hands-on workshops will teach the isolation, culture and manipulation procedures for stem cells and the cells of their regulatory niche. Additional activities include a seminar series with leaders in the field, postdoctoral seminar series, journal clubs, mini- symposia and an annual retreat. The [REDACTED] stem cell program has well-established and active collaborations with the Stem Cell Program at [REDACTED] and the Stem Cell Transplantation Program at [REDACTED]. CIRM trainees from these and other local institutes will be encouraged to attend our courses. Conversely, our trainees will enroll in courses offered by CIRM programs of other institutes. A joint program on ethical issues and other general aspects of stem cell research is planned. Trainees will use multidisciplinary approaches to study important problems in stem cell niche biology and will be mentored by at least two faculty members with distinct expertise. Projects will include (i) the role of the CD44/hyaluronan pathway in regulating the bone marrow hematopoietic niche; (ii) the function of the neural stem cell niche in inflammation; (iii) the role of the adipose microenvironmental niche in obesity; and (iv) biology of the specific microenvironmental niches supporting cancer stem cells. In summary, this program will provide a focused, interactive approach to train junior scientists for independent research on the influence of microenvironmental niche on stem cell biology.

Benefit of this Program to California

This program will benefit the people and the state of California by providing high-quality training in the scientific, clinical, social, and ethical aspects of stem-cell research to the scientists and clinicians who will develop and apply future therapies in this rapidly emerging field.

Summary of Review

This type III proposal seeks funding to train four post-doctoral fellows with a specific focus on stem-cell regulatory microenvironments that affect both fate and pathogenesis in particular disease states. Courses are planned that focus on cell and molecular biology of different lineage and organ-specific niches, and will include experts from other institutions in California and the USA. There is little or no description of an ethics, social, and legal implications course in the training program, other than to state that other institutions nearby can help with this. The program director is an assistant professor with relatively modest experience in mentoring, so there is concern that the director may have difficulty in implementing the program. The administrative structure appears suitable and the institution will allocate 6000 sq ft of laboratory space for routine as well as stem cell-related experiments. Many of the in-house faculty members have been trained as post-doctoral fellows at this institution, speaking for the likely advancement of new trainees. However, the quality of existing training programs and the size and quality of the applicant pool were difficult to ascertain with the available information.

Overall Strengths and Weaknesses

The main strength of this proposal is the important scientific focus on microenvironments for stem-cell research. However, the overall training and research environment is not as rich in depth and breadth as would be desired. The extent to which association with other area institutions might mitigate these deficiencies is not clear from the application. Further, the program director is very junior and may have difficulty implementing the program.

Recommendations

Not recommended for funding at this time.

	Pre	Post	Clinical	Total
Fellows Requested:	0	4	0	4
Fellows Recommended:	0	0	0	0

	Year 1	Total
Budget Requested:	\$ 306,320	\$ 965,515
Budget Recommended:	0	0